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HM22/0619

TURNER, S	EXAMINER
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ART UNIT	PAPER NUMBER
1547	

06/19/01

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

# Office Action Summary

Application No.  
09/207,649

Applicant(s)  
Lindquist

Examiner  
Sharon L. Turner, Ph.D.

Art Unit  
1647



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1) ☒ Responsive to communication(s) filed on 4-4-01

2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

## Disposition of Claims

4) ☒ Claim(s) 1, 3, 7-20, 22, and 37-40 is/are pending in the application.

4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.

6) ☒ Claim(s) 1, 3, 7-20, 22, and 37-40 is/are rejected.

7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.

8) ☒ Claims 38-40 are subject to restriction and/or election requirements.

## Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some\* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

19) ☐ Notice of Informal Patent Application (PTO-152)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_

20) ☐ Other: \_\_\_\_\_

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## **DETAILED ACTION**

### **Response to Amendment**

1. The amendment filed 4-4-01 has been entered into the record and has been fully considered. Claim 4 is canceled. Claims 1, 3, 7-20, 22 and 37-40 are pending.
2. Claims 38-40 remain directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: New claims 38-40 are drawn to methods of identifying candidate substances that inhibit the formation of amyloid fibrils. This is in contrast to methods of identifying candidate substances that inhibit the formation of amyloid aggregates. Fibrils are distinct structures from aggregates because fibrils are ordered structures of beta amyloid found in Alzheimer's brains and exhibit rod-like and beta-sheet conformations. In contrast, aggregates merely constitute clustered, closely associated or bound proteins.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 38-40 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. As a result of applicants amendment, all rejections not reiterated herein have been withdrawn by the examiner.

### ***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 3, 7, 12-13, and 17-18 stand rejected under 35 U.S.C. 102(b) as being anticipated by Hughes et al, PNAS, 93:2065-70, 1996 as set forth in Paper No. 5, mailed 8-4-99. Claims 8-11, 14-16, 19, 20 and 22 are <sup>to</sup> rejected as depending from a rejected base claim.

Applicant argues that the assay employed in the Hughes et al reference measures an interaction between two monomers, and that the system cannot be considered to involve the formation of aggregates.

Applicants arguments filed 4-4-01 have been fully considered but are not persuasive. Contrary to applicants assertion, the Hughes reference clearly measures the interaction of A $\beta$  peptides which aggregate as evidenced in Figure 1. Applicants have not defined aggregates to exclude the interaction of A $\beta$  monomers and as noted by applicants Hughes recognizes that the monomer formation precludes aggregation. The A $\beta$  monomers of Hughes clearly interact as evidenced by the expression of the reporter gene lacZ and that direct interaction constitutes an aggregation as depicted in Figure 1. The conditions appear to be sufficient for aggregation. The A $\beta$  TT mutant is an identified substance which inhibits aggregation. Thus, Hughes anticipates the claimed invention.

6. Claims 1, 3, 15, 17-19 and 37 stand rejected under 35 U.S.C. 102(b) as being anticipated by Cordell et al, WO91/04339, 4 April, 1991. Claims 4, 7-14, 16, 20, 22 and 37 are <sup>ob</sup> <sup>to</sup> rejected as depending from a rejected base claim.

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Applicants argue that Cordell does not teach chimeric beta amyloid peptides and thus cannot anticipate the claimed invention.

Applicants arguments file 4-4-01 have been fully considered but are not persuasive. Applicants definition of chimeric appears to be that of non-naturally occurring. Cordell teaches the substitution of one or more amino acids in the resulting amyloid peptides thus constituting non-naturally occurring peptides which are chimeric peptides as the sequences differ from the naturally occurring sequence.

### **Rejections Necessitated by Amendment**

#### ***Claim Objections***

7. Claim 7 and dependent claims thereof 8-11 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The recitation "at least an aggregate forming domain" broadens the scope of claim 1, in particular to the mammalian aggregat-prone amyloid protein. The peptide which is only to required to comprise "the domain" encompasses alternative amino acid sequences which are not recognized as mammalian amyloid peptides and thus do not further limit but broaden independent claim 1.

#### ***Claim Rejections - 35 USC § 112***

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

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person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 7-11 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for mammalian prion proteins and mammalian amyloid peptides, does not reasonably provide enablement for a mammalian aggregate-prone amyloid protein wherein the protein is a chimeric protein which comprises an aggregate forming domain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specifications disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. Claims 7-11 recite mammalian peptides which are chimeric and comprise an aggregate forming domain. The skilled artisan as taught by Skolnick et al., Trends in Biotech., 18(1):34-39, 2000 recognizes that proteins are highly dependent upon sequence structure and that a single mutation of a protein can affect the biological activities of the molecule. The mutated chimeras contain foreign sequences with divergent structural and functional characteristics. Applicants claims have been clarified as to chimeric peptides which comprise a naturally occurring mammalian aggregate-prone amyloid peptide aggregate forming domain. However, the specification fails to teach the structural and functional characteristics of such sequences which direct aggregate formation. Further the specification fails to teach the experimental methodology for such diverse sequences whereby

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one of skill in the art can readily determine those sequences which are required. Thus, in view of the quantity of experimentation necessary to determine those sequences which are required of a chimera, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to make and use the sequences as claimed.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 7-11 are rejected under 35 U.S.C. 112, second paragraph, as set forth in Paper No. 14 mailed 10-24-00 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 7-11 are indefinite as the skilled artisan is not reasonably apprised of the metes and bounds of "an aggregate forming domain." The skilled artisan has no guidance by which to determine that portion of a chimeric protein which forms "an aggregate forming domain."

Applicants argue in response to the previous rejection that one of skill in the art would have known such to refer to amino acids which are involved in aggregation and that because one of skill in the art would have to figure out what portions of the aggregate prone amyloid protein constitutes an aggregate forming domain does not render the claim indefinite because the specification is clear as to its intent and identifies ways of determining whether a protein aggregates, in particular at p. 13, lines 2-3.

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Applicants arguments filed 4-4-01 have been fully considered but are not persuasive.

Page 13, lines 2-3 merely points out various methodologies for detecting aggregation. However such assays as Congo Red staining and birefringence fails to identify the sequences which are required for the formation of aggregates and the skilled artisan is not apprised of the metes and bounds of the sequences encompassed by the claims.

12. Claims 1, 3, 7, 12-13, 17-18 and 37 are rejected under 35 U.S.C. 102(e) as being anticipated by Findeis et al., US Patent No. 5854,204 filed 3-14-1996.

Findeis et al., teach A-beta peptides including chimeric peptides which differ from naturally occurring beta amyloid sequences and screening assays to identify modulatory influences on amyloid aggregation. The peptides may be biotinylated, labeled by fluorescence, or monitored in seeded assays. The peptides include those of Tables 1-VI and Examples 1-12 in particular. Thus the reference teachings anticipate the claimed chimeric peptides.

*neglected pp. 44-45 previous is at col 38 lines 51-52 and col 38 lines 60-65*  
*Chemical col 30, lines 47-48*

#### Status of Claims

13. No claims are allowed.

#### Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37



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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.  
June 17, 2001

**CHRISTINE J. SAUD  
PRIMARY EXAMINER**

*Christine J. Saud*